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THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of
 Roland A. Carlsson et al.
 Serial No. 09/734,801
 Filed: December 12, 2000
 For: A METHOD FOR IN VITRO
 MOLECULAR EVOLUTION OF
 PROTEIN FUNCTION

) Group Art Unit: 5194
)
) Examiner: S. Chunduru
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) Response to Paper No. 8
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DECLARATION OF CARL BORREBAECK

I, Carl A.K. Borrebaeck, hereby declare that:

1. I am a citizen of Sweden and reside at Ättevägen
 8B, 245 62 Hjärup, Sweden.

2. I received a M.S. degree in Chemical Engineering
 and a Ph.D. degree in Biochemistry 1979 (with a subspecialty in
 Molecular Immunology), respectively, from Lund University. I
 have been a member of the faculty of Lund University since 1982.
 I am currently a Professor and Chairman in the Department of
 Immunotechnology at Lund University. The details of my
 education and professional history are set forth in my
 curriculum vitae, attached hereto as Exhibit A.

3. I have over twenty-five years of experience in the
 field of immunology, my particular area of expertise being in
 molecular immunology/biology.

4. I am the author or co-author of 178 scientific
 articles on the subjects of biochemistry, immunology, and
 immunotechnology. A list of these articles is set forth in my

Curriculum vitae, attached hereto. My current areas of research involve the development of methods for generating novel polynucleotides and encoded polypeptides thereof, the generation of agents having utility for antibody based immunotherapy, and the use of protein microarrays in target discovery assays.

5. I am a co-inventor of the subject matter disclosed and claimed in U.S. Patent Application Serial No. 09/734,801, entitled "A METHOD FOR IN VITRO MOLECULAR EVOLUTION OF PROTEIN FUNCTION." (hereinafter "the '801 application").

Statements Regarding Issues Related to Judicially Created Doctrine of Obviousness-Type Double Patenting, Anticipation, and Obviousness

6. I have read and am familiar with the Official Action dated April 16, 2002, in the '801 application. I understand the nature of the rejections made by the Examiner concerning the doctrine of obviousness-type double patenting, anticipation, and obviousness. I have also read the references cited in connection with the rejections set forth in the Official Action of April 16, 2002. In particular, I understand that it is the Examiner's position that the claimed invention is inherent in the teachings and anticipated by the disclosure of U.S. Patent No. 6,159,690 and obvious in view of U.S. Patent No. 5,811,238 (hereinafter referred to the '238 patent) considered in combination with Berger (1994, *Analyt Biochem* 222:1-8).

7. As exemplified in the specification, my co-inventors and I have devised an improved method for the generation of novel polynucleotides and polypeptides encoded thereby, wherein such novel products may be selected for advantageous properties. The improved method involves the use of single stranded, as opposed to double stranded, DNA in gene shuffling methods to provide superior frequencies of functional recombinant end-products.

In order to provide improved methods for gene shuffling, different experimental parameters were varied to investigate the impact of such changes on the functional outcome of the process. As described hereinbelow, experiments were performed to compare the utility of single stranded versus double stranded DNA in the methods of the present invention. Of note, there is a strong tendency for double stranded fragmented genes to form homoduplexes rather than heteroduplexes upon PCR-mediated recombination. Clearly, the formation of homoduplexes would lead to the re-generation of the parent polynucleotides and thus, render the process of limited utility for the production of novel polynucleotide sequences. When engineering novel polynucleotides by shuffling different family member genes, therefore, it is important to achieve an efficient recombination frequency in order to optimize the diversity of the end-product shuffled polynucleotides.

In order to evaluate the effects of altering various experimental parameters on recombination frequency among family member genes, three different scFv antibody fragments (CT17, SMUC, and F8) were used as starting material for DNA shuffling. These scFvs differ only in the six hypervariable loops. For these experiments, double stranded and single stranded polynucleotides encoding each of the three scFv antibodies were isolated. For clarity, the procedures for double stranded and single stranded polynucleotide starting material will be described separately. An equimolar mixture of the three scFv double stranded polynucleotides was used in fragmentation reactions and fragmented double stranded polynucleotides reassembled by PCR to produce full length genes. For single stranded shuffling experiments, plus and minus strand populations for each of the scFv fragments were generated by PCR amplification. The plus strand was amplified using a

biotinylated primer, the incorporation of which facilitated the isolation of the biotinylated plus strand PCR product using streptavidin-magnetic beads. The complementary strand, the minus strand, was also amplified in parallel using an unbiotinylated primer. The minus strand PCR product, therefore, remained in solution after affinity purification of the biotinylated plus strand with streptavidin-magnetic beads. Equimolar mixtures comprising either the plus strands or the minus strands of the three scFv polynucleotides were generated. The plus and minus single stranded polynucleotide population mixtures were digested separately to produce plus and minus single stranded fragments. The resultant fragmented plus and minus single stranded populations were subsequently mixed and reassembled by PCR to produce full length genes. Shuffled full length genes derived from double stranded or single stranded starting material were subcloned and individual clones sequenced. An optimum in recombination frequency was identified, which was dependent on the duration time of fragmentation. See Exhibit B.

These experiments revealed the surprising result that the frequency of clones having at least one recombination event was significantly higher for shuffled single stranded digested polynucleotide populations than for shuffled double stranded digested polynucleotide populations. Sixty percent of the clones derived from shuffling single stranded starting material had a least one recombination, whereas only forty percent of such recombinants was obtained following shuffling of double stranded starting material. Of note, high recombination frequency is the basis for an efficient shuffling technology. See Exhibit B.


The foregoing data clearly show the superior and unexpected results for producing polynucleotide variants

achieved using exonucleolytic digestion of single stranded DNA as the starting material in DNA shuffling methods of the present invention.

8. The experimental data provided in Exhibit B and the methodology provided in the '801 application, set forth clear evidence that the use of single stranded DNA in DNA shuffling protocols provides an unexpected advantage over the use of double-stranded DNA for the generation of novel and improved polynucleotides and polypeptides encoded thereby. This method differs significantly from that disclosed in the '690 patent as no template is employed. Furthermore, one of skill in the art would not have been motivated to alter the method of Stemmer or the method of Berger to arrive at the presently claimed invention as these methods rely on the use of double stranded DNA as starting materials. Additionally, there is no teaching or suggestion of the advantages of using single stranded DNA as a starting material to generate improved polypeptide encoding nucleic acids via gene shuffling as set forth in Exhibit B in either of these references.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the above-referenced application or any patent issued thereon.

2002-08-05
DATE



Carl A.K. Borrebaeck
CARL A. K. BORREBAECK
Professor
Dept. of Immunotechnology
University of Lund, Sweden

99-11-30

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<http://www.kc.lth.se/immun/default.html>

Home Address:

Ättevägen 8B
S-245 62 Hjärrup
Sweden
Phone: +46-40-46 22 46

Personal:

Date and Place of Birth: October 21, 1948, Halmstad, Sweden.
Marital Status: Married 1981 to Camilla Brunnby, B.Sc., three children.
Citizenship: Swedish

Languages:

English, German.

Education:

1966-69 Halmstad Highschool of Technology (Tekniskt gymnasium).
1971-74 University of Lund, Lund, Sweden, B.Sc. (Mathematics, Biochemistry, Physics).
1974-76 Lund Institute of Technology (LTH), M. Chem. Eng. (Chemistry/Biochemistry).
1976-79 Lund University/Lund Institute of Technology, D.Sc. (Biochemistry, with special emphasis on Molecular Immunology).

Senior Academic Positions:

1980-1981 Visiting Scientist/Postdoctoral Fellow, Department of Biochemistry, University of California, Davis, USA (with Professor Marilyn E. Etzler).
1981-1984 Senior Research Associate (Forskningsassistent), Department of Pure and Applied Biochemistry, Lund University.
1982-1984 Assistant Professor of Biochemistry (Oavlonad Docent), Department of Pure and Applied Biochemistry.
1984 Deputy Professor of Biochemistry (T.f. Professor), Department of Pure and Applied Biochemistry.
1985 Deputy Associate Professor of Immunotechnology (T.f. Docent), Department of Biotechnology, Lund University.



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1985-1989	Associate Professor of Immunotechnology (Docent), Department of Biotechnology.
1989	Deputy Professor of Immunotechnology (T.f. Professor), Department of Biotechnology.
1990- 1994-1998	Professor of Immunotechnology, Department of Immunotechnology. Deputy Chairman of the Wallenberg Laboratory, Lund University.
1998-2000	Chairman of the Wallenberg Laboratory, Lund University
1996-1997	Nominated and selected as OMRF Esther Z. Greenberg Scholar, Oklahoma Medical Research Foundation, Oklahoma City.
1998	September 1998 as Visiting Greenberg Professor, Oklahoma Medical Research Foundation, Oklahoma City.

Board Member of National Research Councils:

1996-2000	The Swedish Research Council for Engineering Sciences (TFR), Executive Board Member
1999-2000	Chairman Biotechnology Section, The Swedish Research Council for Engineering Sciences (TFR) Executive Board
1999	Inter- Research Council Working Party on Functional Genomics
1999	National Committee for Molecular Biology (representative of TFR)

Industrial & Financial experience:

1. Company Boards:

1983-presently	Cofounder and Board Member of BioInvent International AB, Lund, Sweden.
1-1993	Board member Pronova Oncology (Oslo)
1-2000	Board member of Innovation Stipend Selection Committee (Teknikbrostiftelsen)
1998-	Board Member Teknikbrostiftelsen (Technology Transfer Foundation)
1998-	Chairman of the Board, Lund University Technology Group, (Forskarpatent i Syd AB)
1-2000	Board Member Teknopol AB (Lund University Business Consulting)
2000 -	Board Member TeknoSeed AB (Seed Capital Investments)
2001-	Cofounder and Board Member of Alligator Bioscience AB, Lund, Sweden

2. Operative Industrial Positions

1987-	Senior Vice President - CSO, BioInvent Int. AB.
1-1994	President & CEO, BioInvent Int. AB.

3. Scientific Advisory Boards:

1-1994	Member of the Research Selection Committee of Pronova A/S
2000-2003	Scientific Advisory Board to Academy of Finland for the Finnish Center

of Excellence: VTT Industrial Biotechnology

4. Financial and Capital Market experience:

- 1-1995 Research consultant to major/intermediate pharmaceutical companies in USA and Sweden.
- 1999- Advisory Board Member to InnovationsKapital AB (Venture Capital)

Selected European Commission Awards

- BIO2-CT92-0269 "In vitro immunization of human B lymphocytes", total grant 15 MSEK
- BIO4-CT95-0252 "Immunological engineering for generation of human therapeutic antibodies", total grant 18 MSEK
- BIO4-CT96-0246 "Development of in vitro tests for drug allergenicity and B cell switching to IgE synthesis, total grant awarded 14 MSEK.
- PL960389 Concerted action "The biotechnological use and further development of phage display", total grant awarded: 5 MSEK.
- BMH4-97-2131 "Targeted anti-CD40 monoclonal antibodies for treatment of multiple sclerosis", total grant awarded: 6 MSEK
- QLK3-2000-00273 "Human cell systems for predicting the allergenicity of genetically engineered proteins", total grant awarded 13 MSEK.

University Service:

Faculty representative in University policy issues:

- 1997-1998 Faculty representative in the working party forming the University policy for Patent and Commercialization of Research.
- 1997-1998 Faculty representative in the working party forming the University policy for the University Research Policy
- 1998-2000 Board member of the Biomedical Graduate School of Research

Executive examiner of Doctorate Degrees (Fakultetsopponent):

- 1991-1992 Per Borup Christensen (Doctorate Degree (Ph.D.)), Title: Human monoclonal antibodies against colo-rectal cancer associated antigens of potential value in diagnosis and therapy of cancer. Odense University, Denmark.
- 1998 Vigdis Luvrak (Ph.D.), Title: Filamentous phage peptide-display: A tool in the study of macromolecular interactions. Oslo University, Norway
- 2000 Ulrik Bjerl Nielsen (Ph.D.), Title: Antibody Targeted Breast Cancer Therapy. University of Copenhagen, Denmark.

Supervisor and Examiner for Graduate Degrees:

- 1988 Susanna A. Möller (Doctorate Degree in Biotechnology) (Tekn. Dr.), Title:

- Development of in vitro immunization for the production of mouse and human monoclonal antibodies.
- 1989 Ulf Schröder (Doctorate Degree in Biochemistry) (Tekn. Dr.), Title: Starch microspheres.
- 1990 Lena Danielsson (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Human monoclonal antibodies: In vitro immunization and cloning of DNA encoding variable regions.
- 1992 Mats Ohlin (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Human monoclonal antibody technology: A tool to investigate human antibody repertoires.
- 1993 Karin Kristensson (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: T cell mediated effects on in vitro B cell response.
- 1994 Li-te Chin (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Site-directed in vitro immunization: A model for sequential antigen-specific activation of human B cells.
- 1995 Marta Dueñas (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Phage display and bacterial expression of antibody fragments.
- 1995 Cristina Mårtensson-Eriksson (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: The Scid Mouse. A tool for generation of human monoclonal antibodies.
- 1995 Peter Ifversen, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Human antibody technology. An evaluation of the Scid-hu-PBL model.
- 1996 Ann Catrin Simonsson Lagerkvist, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: In vitro generation and selection of antigen-specific antibodies
- 1996 Christina Furebring, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Regulations of Ig genes.
- 1996 Ann Christin Malmberg, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Molecular recognition in antibody engineering, Studies of recombinant and phage displayed antibodies.
- 1996 Marie Wallén Öhman, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: MHC class I induced apoptosis in hematopoietic cells.
- 1998 Sigurdur Ingvarsson, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Signalling mechanisms in B cell differentiation: Studies on specific human immune response in vitro.
- 1998 Katarina Dahlenborg, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Cellular and Molecular Aspects on Germinal Center Reactions
- 1998 Eva Andersson, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Studies of T- and B cells for the generation of human antigen specific antibodies
- 1993 Nina Nilsson, (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: In vivo and in vitro evolution of molecular mechanisms.
- 2000 Camilla Ottosson (Licentiat Degree in Immunotechnology)(Tekn. Lic.), Title: In vitro evolution by the FIND system and selection of novel phage antibodies.
- 2000 Magnus Strandh (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Insights into weak affinity antibody-antigen interactions.

- 2000 Pernilla Jirholt (Doctorate Degree in Immunotechnology) (Tekn. Dr.), Title: Generation and evolution of human antibody fragments – the CDR shuffling approach.

Qualifying Examination Committee (betygsnämnd):

- 1988 Michael Dohlsten (Doctorate Degree in Medical Science), Dept of Tumor Immunology, Title: Suppressive effects of histamine on T cell activation.
- 1988 Susanne Flygare (Doctorate Degree in Biochemistry), Dept of Pure and Applied Biochemistry, Title: I. Steroid transformation using immobilized cells. II. Affinity precipitation and magnetic aqueous two phase separation.
- 1988 Tyri Valdimarsdottir (Tekn. Lic.), Dept of Food Chemistry, Title: Quantitative determination of water soluble pentosans of rye grain. An immunochemical approach.
- 1989 Gunnar Hedlund (Doctorate Degree in Medical Science), Dept of Tumor Immunology, Title: Phenotype and function: Studies on T lymphocytes in rat and man.
- 1989 Bo Jansson (Doctorate Degree in Medical Science), Dept of Tumor Immunology, Title: Tumour associated antigens of chemically induced rat colon carcinomas defined by rat antibodies.
- 1990 Jan-Ingvar Jönsson (Doctorate Degree in Medical Science), Dept of Tumor Immunology, Title: Accessory molecules in T lymphocyte activation: The role of CD4 and CD8.
- 1991 Lars I. Andersson (Doctorate Degree in Biochemistry), Dept. of Pure and Applied Biochemistry, Title: Molecular recognition in synthetic polymers.
- 1992 P-O Ericsson (Doctorate Degree in Medical Science), Dept of Tumor Immunology, Title: Functional analysis of rat lymphocytes subsets.
- 1993 Karin Kronkvist (Doctorate Degree in Analytical Chemistry), Dept. of Analytical Chemistry, Title: Determination of steroids in biosamples at picomolar levels using enzyme immunochemical methods.
- 1994 Johan Hansson (Doctorate Degree in Medical Science), Dept of Tumor Immunology, Title: Activation and differentiation of cytotoxic T lymphocytes.
- 1995 Karin Johansson (Doctorate Degree in Medical Science), Dept of Immunology, Title: Analysis of Immunoglobulin gene expression: Focus on Oct2.
- 1996 Michael Garkavij (Doctorate Degree in Medical Science), Dept. of Radiophysics, Title: Improving radioimmunotargeting of tumors.
- 1998 Margareta Krook (Doctorate Degree in Biochemistry), Dept of Pure and Applied Biochemistry, Title: Combinatorial Methodology.
- 2000 Alexander Rosendahl (Doctorate Degree in Medical Science), Dept. Cell and Molecular Biology, Lund University, Title: Tumor Targeted Super Antigens.
- 2000 Gabriela Godaly (Doctorate Degree in Medical Science), Dept. of Medical Microbiology, Lund University, Title: Mechanisms of E. coli induced transepithelial neutrophil migration"
- 2000 Jesper Tordsson (Doctorate Degree in Medical Science), Dept of Tumor Immunology, Title: Identification of tumor associated antigens by antibodies phage selected using tumor cells and tissue sections.

International Promotion Review Boards:

- 1986 Prof. Irvin Goldstein, Department of Biological Sciences, University of Michigan, Ann Arbor, USA.
1991 Assistant Professor Steven Foug, Department of Pathology, Stanford University, Stanford, USA.
1997 Privaten Dozent for Stefan Dübel, Germany
1999 Senior Lecturer John Coleman, University of Liverpool, U.K.

Extra Curriculum Services:

- 1987-89 Grant reviewer for Bundesministerium für Wissenschaft und Forschung, Vienne, Austria
1990 Referee for the Swedish Nobel Committee.
1993 Grant reviewer for The Israel Science Foundation.
1994 Grant reviewer for Biotechnology and Biological Sciences Research Council (BBSRC) (U.K.).
1995 Grant reviewer For Human Frontier Science Program
1995- Grant Review Board for Teknikbröstförelsen (Foundation for Science Transfer between University & Industry)
1996 Grant reviewer for the Danish Cancer Society
1996 Grant reviewer for Pioneer Grant by NVO, The Netherlands

Editorial Services:

Editor-in-Chief:

1995-1998 IMMUNOTECHNOLOGY, Elsevier Science Publishers.

Editorial Board:

European R&D Database, Bowker Sauer.
Human Hybridomas and Antibodies (Editor-in-Chief: Mark Glassy), Butterworth Publishing
Journal of Clinical Laboratory Analysis (Editor-in-Chief: Ralph Reisfeld)
Serodiagnosis & Immunotherapy in Infectious Disease (Editor-in-Chief: James Burnie), Butterworth-Heinemann Ltd.

Editorial Reviewer for:

Proc. Natl Acad Sci. (USA), Nature Biotechnology, Eur. J. Immunol., Immunology, J. Immunol. Methods, Molec. Immunol., Anal. Biochem., Eur. J. Biochem., FEBS Letters, Glycoconjugate J., Arch. Biochem. Biophys, Hybridoma, Chimaoggia, Biotechniques etc.

Editor of:

"In Vitro Immunization in Hybridoma Technology", Elsevier Science Publishers, Amsterdam (1988), 317 pages.

- "Electromanipulation in Hybridoma Technology", Stockton Press (1989), co-editor: Inger Hagen, SI, Oslo, Norway.
 "Therapeutic Monoclonal Antibodies", Stockton Press (1990), co-editor: James W. Larrick, Genelabs Inc., California.
 "Antibody Engineering Manual", W.H. Freeman Publishing Co. 1st Ed., 1991.
 "Antibody Engineering Manual", Oxford University Press. 2nd Ed., 1995.

Invited speaker and chairman at scientific meetings:

- 1978 "Non-equilibrium enzyme immunoassay" at the Enzyme Labelled Immunoassay of Hormones and Drugs, Ulm, FRG.
 1983 "Mitogenic properties of PHA isolectins" at the Special Conference on Chemical Taxonomy, Molecular Biology and Biological Function of Lectins, Asilomar, California.
 1986 "In vitro immunization in hybridoma technology" at the XVII Meeting of Scandinavian Society for Immunology, Tampere, Finland. Chairman
 1986 "In vitro immunization for the production of monoclonal antibodies" at the Swedish Academy of Pharmaceutical Sciences, Stockholm.
 1986 "Hybridoma technology. Future developments in the production of murine and human monoclonal antibodies" at the Annual Meeting of the Swedish Society for Clinical Chemistry, Helsingborg, Sweden.
 1987 "In vitro immunization of peripheral blood lymphocytes for the production of human monoclonal antibodies" at the International Symposium on In Vitro Immunization in Hybridoma Technology, Tylösand, Sweden. Chairman.
 1987 "Human and mouse monoclonal antibodies produced by in vitro immunization" at The Annual Meeting of the Danish Society for Engineering, Copenhagen.
 1989 "Production and characterization of human monoclonal antibodies derived by in vitro immunization" at the International workshop on monoclonal antibody technology, Havana, Cuba.
 1989 "Human monoclonal antibodies. Production and therapeutic potentials" at the Second IRI Biotechnology Conference, Edinburgh, U.K.
 1989 "Strategies for the production of human monoclonal antibodies" at 2nd Japanese Assoc. for Animal Cell Culture, Tsukuba, Japan.
 1989 "Human monoclonal antibodies" at the Third Conference on Immunity to Cancer, Williamsburg, Virginia, USA.
 1989 "In vitro immunization for the production of human monoclonal antibodies" at the Contact Group on Monoclonal Antibodies (National Science Foundation), Liège, Belgium.
 1990 "Combination of cell and molecular biology approach for the production of human monoclonal antibodies", 8th European Immunology Meeting, Edinburgh, Scotland.
 1990 "In vitro immunization and human monoclonal antibodies", IBC Meeting, London, U.K.
 1990 "Scid-hu - Generation of human antibody specificities", Immunotechnology Conference, The Danish Society for Engineering, Copenhagen.

- 1991 "Advances in the application of monoclonal antibodies in clinical oncology", 8th International Hammersmith Meeting, Porto Carras, Halkidiki, Greece.
- 1992 "Tools for the production of human monoclonal antibodies", BIOTECH92, Genua, Italy.
- 1992 "The scid-hu model in human hybridoma technology", 2nd International Conference on Human Antibodies and Hybridomas, Cambridge, U.K.
- 1992 "Novel approaches for the production of human monoclonal antibodies", The 3rd International Conference on Biotechnology and Genetic Engineering, Havana, Cuba.
- 1992 "Human monoclonal antibodies: Tool and technologies", FEBS Meeting, Dublin, Ireland.
- 1992 "Manipulation of antibody specificities using scid-hu-mice", 3rd IBC Conference on Antibody Engineering, San Diego, USA.
- 1992 "Overview of issues, options & challenges for human monoclonal antibodies", IBC Conference on Human Monoclonal Antibodies, San Diego, USA
- 1993 "Recent developments in the generation of natural human monoclonal antibodies", Therapeutic Antibodies, Tokyo, Japan
- 1993 "Recent progress in the development of human monoclonal antibodies", 8th International conference on monoclonal antibody immunoconjugate for Cancer, San Diego, USA.
- 1993 "Antibody technology and phage display: Possibilities and limitations", Swedish Academy of Pharmaceutical Sciences, Stockholm, Sweden
- 1993 "Mimicking the humoral immune response: Linking antigen recognition and phage replication", 4th IBC Conference on Antibody Engineering, San Diego, USA.
- 1994 "Antibody Engineering", IMLAB Conference, Stockholm
- 1994 "SAP selection of phage displayed antibodies", Swedish Society for Biochemistry and Molecular Biology, Lund
- 1994 "SAP selection of phage displayed antibodies derived from in vitro immunized human B cells are affinity matured", European Immunology Meeting, Barcelona, Spain.
- 1994 "Mimicking the humoral immune response in vitro", Scheele Symposium, Uppsala, Sweden
- 1994 "Phage displayed antibodies derived from primary and secondary in vitro immunization" Biotechnologia 94, Habana, Cuba
- 1995 "SAP-Homogeneous selection of phage libraries", Nationaal Faag Display Platform, Maastricht, NL.
- 1995 "Phage display and its application to in vitro immunized human cells", 4th Int. Conference on Human Antibodies and Hybridomas, Amsterdam, The Netherlands
- 1995 "Homogeneous kinetic selection in antibody phage libraries", 23rd FEBS Meeting, Basel, Switzerland
- 1995 "Homogeneous selection principles in antibody phage libraries", Therapeutic Antibody Technology 95, San Fransisco, USA

- 1995 "Recombinant technologies for generation of human antibodies" Nobel Forum, Stockholm, Sweden
- 1996 "Homogeneous selection of phage libraries" Keystone Symposium, Taos, N.M., USA
- 1996 "Selection by bacteriophage infection. Technologies for gene identification", The Nordic Network Program on Immunotechnology, Helsinki, Finland.
- 1996 "Bacterial and phage display of molecular libraries: Design and applications", Oklahoma Medical Research Foundation, OKC, USA
- 1997 "Primary and secondary in vitro immunization of human B cells: Evaluated by phage display", University of Texas Southwestern Medical School, Dallas, TX.
- 1997 "Combination of bacterial and phage display for potential gene identification", IBC Conference "Exploiting display technologies in drug discovery, molecular evolution and vaccine development", Lake Tahoe, CA, USA.
- 1997 "Antibody based cancer therapy: A viable concept?" Oklahoma Health Science Center, OKC, OK
- 1997 "Selective Infection Mediated by Protein-Ligand interactions: Tapping the potential of molecular libraries for gene identification", Wennergrens Symposium on Chemical & Biological Combinatorial Libraries, Stockholm
- 1997 "Molecular libraries in functional genomics", Biotechnologia La Habana 1997, Havana, Cuba
- 1998 "Molecular libraries in functional genomics", Analytica 98, München.
- 1998 "Phage and Bacterial display", Workshop - European Science Foundation, Brussels
- 1998 "Design of molecular libraries in functional genomics", IBC Conference on Antibody Engineering, San Diego, USA
- 1999 "Deciphering the role of phage protein 3 during bacterial infection - implications for selective infection", Biotechnologia La Habana 1999, Havana, Cuba
- 2000 "n-CoDeR - A novel library design", Workshop on Biomolecular Recognition within Proteomics, Stockholm, Sweden
- 2000 "Protein chips for proteome analysis", Mini-symposium: Chips and Proteome Analysis, Malmö, Sweden
- 1991 "Postgenome research - A challenge " Biotech Forum, Ystad
- 1997 "Postgenomic challenges - Design of a novel antibody library concept", DeCode Genetics, Reykavik, Iceland.
- 2000 "Biomolecular recognition", VTT, Espoo, Finland.

Organizing Committees:

- 1986-
- 1989 Co-organizer of the Annual Meeting for "Lunda Immunologer", appr. 50 participants.
- 1987 Organizer of "International Symposium on In Vitro Immunization in Hybridoma Technology", Tylösand, Sweden, 85 participants (limited) from 16 countries.

- 1988 Scientific committee member of BioScience 88, Malmö, Sweden, appr. 700 participants.
- 1988 Co-organizer of "Electrofusion in Hybridoma Technology", Oslo, Norway 55 participants (limited) from 11 countries.
- 1989 Scientific committee member of BioScience 89, Malmö, Sweden, appr. 800 participants (chief organizer of a Monoclonal Antibody Workshop during BioScience).
- 1990 Scientific advisory committee of First Conference on Human Hybridomas and Monoclonal Antibodies, Orlando, Florida, USA.
- 1990 Workshop organizer/chairman at the 8th European Immunology Meeting, Edinburgh, Scotland.
- 1991 Workshop organizer/chairman at the 9th European Immunology Meeting, Helsinki, Finland.
- 1992 Scientific advisory committee of Second Conference on Human Hybridomas and Monoclonal Antibodies, Cambridge, U.K.
- 1992 Scientific advisory committee of the 3rd IBC Conference on Antibody Engineering and IBC Conference on Human Monoclonal Antibodies, San Diego, USA.
- 1993 Scientific advisory committee of Third Conference on Human Hybridomas and Monoclonal Antibodies, San Antonio, TX. USA.
- 1993 Scientific advisory committee of the 4th IBC Conference on Antibody Engineering, San Diego, USA.
- 1994 Workshop organizer/chairman at the 11th European Immunology Meeting, Barcelona, Spain.
- 1994 Scientific advisory committee of the Fourth Conference on Human Hybridomas and Monoclonal Antibodies, Amsterdam, The Netherlands.
- 1996 Scientific advisory committee of the Fifth Conference on Human Hybridomas and Monoclonal Antibodies, Israel

Society membership:

Scandinavian Society for Immunology
 Swedish Immunology Society
 American Association for the Advancement of Science - Member
 New York Academy of Sciences

Miscellaneous:

Recipient of ICRETT Travel Award (International Union Against Cancer).

PUBLICATIONS

(Experimental papers, reviews, book chapters, patents)

Basic science in red /Applied science in black

Carl A.K. Borrebaeck

1. 1977 Mattiasson, B., Borrebaeck, C., Sanfridsson, B. & Mosbach, K.
Thermometric enzyme linked immunosorbent assay: TELISA.
Biochim. Biophys. Acta 483, 221-227.
2. 1978 Mattiasson B. & Borrebaeck, C.
An analytical flow system based on reversible immobilization of enzymes
and whole cells utilizing specific lectin-glycoprotein interaction.
FEBS Lett. 85, 119-123.
3. 1978 Borrebaeck, C., Börjesson, J. & Mattiasson, B.
Thermometric enzyme linked immunosorbent assay in continuous flow
systems: Optimization and evaluation using human serum albumin as a
model system.
Clin. Chim. Acta 86, 267-278.
4. 1978 Mattiasson, B., Svensson, K., Borrebaeck, C., Jonsson, S. & Kronvall, G.
Non-equilibrium enzyme immunoassay of gentamicin.
Clin. Chem. 24, 1770-1773.
5. 1978 Borrebaeck, C., Mattiasson, B. & Svensson, K.
A rapid non-equilibrium enzyme immunoassay for determining serum
gentamicin.
In: **Enzyme Labelled Immunoassay of Hormones and Drugs**, Ed. S.B.
Pal, Walter de Gruyter & Co., Berlin, pp. 15-27.
6. 1978 Mattiasson, B. & Borrebaeck, C.
Non-equilibrium, isokinetic enzyme immunoassay of insulin using reversibly
immobilized antibodies.
ibid pp. 91-105.
7. 1979 Borrebaeck, C.
Biospecific molecular interactions as a tool in analytical biochemistry;
Illustrated by antibody-antigen and lectin-carbohydrate reactions.
D.Sc. (Doctor of Science), University of Lund, Lund, Sweden.
Doctoral Thesis
8. 1979 Borrebaeck, C. & Mattiasson, B. Recent development in heterogeneous
enzyme immunoassay. (Review)

J. Solid Phase Biochem. 4, 57-67.

9. 1980 Borrebaeck, C. & Mattiasson, B.
A binding assay of carbohydrates and glycoproteins using a lectin electrode.
Protides of the Biological Fluids 27, 607-610.
10. 1980 Borrebaeck, C. & Mattiasson, B.
Competitive bindings studies of lectin-carbohydrate interactions using a lectin electrode.
Enzyme Engineering 5, 193-196.
11. 1980 Borrebaeck, C. & Mattiasson, B.
A study of structurally related binding properties of Concanavalin A using differential scanning calorimetry.
Eur. J. Biochem. 107, 67-71.
12. 1980 Borrebaeck, C. & Mattiasson, B.
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